

Electrochemical Biosensors for Disease Diagnostics

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Abstract

Electrochemical biosensors have emerged as one of the most promising tools for disease diagnosis because they combine high sensitivity, rapid response, portability, and low cost in a single analytical platform. In recent years, growing interest in early disease detection has pushed researchers to develop biosensors that can detect clinically important biomarkers in blood, saliva, urine, sweat, and other biological fluids. These sensors work through the interaction between a biological recognition element, such as an enzyme, antibody, aptamer, or nucleic acid, and a target analyte, which produces an electrical signal that can be measured and correlated with disease status. Recent advances in nanomaterials, flexible substrates, and wearable formats have significantly improved sensor performance, making them more suitable for point-of-care testing and decentralized healthcare. However, despite strong laboratory results, many devices still face challenges related to selectivity, reproducibility, biofouling, and validation in real clinical samples. This report reviews the fundamental principles, recent developments, major applications, and current limitations of electrochemical biosensors in disease diagnosis, with attention to both their scientific progress and their future clinical potential.

Keywords: Electrochemical biosensors, composition, mechanism, applications, biomarkers

INTRODUCTION

Electrochemical biosensors are devices that convert biological reactions into electrical signals for detecting different substances or disease markers. They are widely used in modern diagnostics because they provide fast, accurate, and cost-effective results. These biosensors are especially important for the early detection of diseases, such as diabetes, cancer, and infections, where timely diagnosis is necessary for proper treatment [1]. Unlike traditional diagnostic methods, which are often expensive and time-consuming, electrochemical biosensors offer rapid and portable testing solutions. These biosensors work by combining biological recognition elements with electrochemical techniques. When the target

molecule interacts with the sensor surface, it causes measurable changes in current, voltage, resistance, or conductivity. Due to their high sensitivity and selectivity, electrochemical biosensors can detect even very small amounts of analytes [2]. Different types of electrochemical biosensors include amperometric, potentiometric, conductometric, and impedimetric sensors. Compared to other sensing technologies, they provide excellent sensitivity, easy operation, and suitability for portable diagnostic devices [3].

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Received Date: May 25, 2026

Accepted Date: May 30, 2026

Published Date: June 02, 2026

Citation: Suhavana Devi, Naisergik Deepika Khanna. Electrochemical Biosensors for Disease Diagnostics. Nano Trends: A Journal of Nanotechnology and Its Applications. 2026; 28(2): 43–54p.

BACKGROUND OF THE TOPIC

Disease diagnosis is vital in healthcare because early and accurate detection directly affects treatment outcomes, yet conventional tests are often

slow, costly, and centralized. Electrochemical biosensors offer a practical alternative by enabling rapid, sensitive detection of disease biomarkers from small, minimally processed samples such as blood, saliva, or urine [4]. These devices convert specific biological recognition events typically involving antibodies, enzymes, or aptamers into measurable electrical signals suitable for real-time analysis. Their portability and ease of miniaturization make them ideal for point-of-care use in clinics, homes, and resource-limited settings, reducing dependence on large laboratories and highly trained staff. Modern electrochemical biosensors can be integrated with microfluidic systems to automate sample handling and improve speed, reliability, and throughput [5]. They are also increasingly combined with digital and wireless platforms, allowing data to be transmitted, stored, and analyzed remotely for quicker clinical decision-making and personalized monitoring. Overall, these features support routine screening and large-scale diagnostic campaigns while keeping systems compact, low-cost, and user-friendly [6].

Importance of the Topic

The importance of electrochemical biosensors lies in their potential to support early diagnosis, continuous health monitoring, and faster clinical decision-making. They are particularly valuable in diseases, such as diabetes, cancer, cardiovascular disorders, and infectious diseases, where quick identification of biomarkers can improve patient outcomes [7]. Compared with conventional laboratory techniques, these biosensors are often simpler, more portable, and more affordable, making them attractive for hospitals, clinics, and home-based testing. Their growing relevance is linked to rising demand for personalized medicine and noninvasive diagnostics, plus multiplexed detection of multiple biomarkers from one sample for enhanced accuracy. Compatibility with wearable and implantable platforms enables long-term, noninvasive monitoring of chronic conditions, integrating diagnostics with personalized treatment and digital health ecosystems [8, 9].

Current Relevance

Electrochemical biosensors are highly relevant today because healthcare systems are increasingly moving toward decentralization, early intervention, and digital monitoring. The COVID-19 pandemic further highlighted the need for rapid, portable, and reliable diagnostic technologies, which brought biosensor research into sharper focus.

At the same time, advances in nanotechnology, wearable devices, and miniaturized electronics have opened new possibilities for more sensitive and user-friendly biosensing platforms [9]. As a result, electrochemical biosensors are now being actively explored not only for laboratory research but also for real-world diagnostic use. Moreover, their low cost and ease of fabrication make them ideal for resource-limited settings. They offer high selectivity and sensitivity through biorecognition elements like enzymes and antibodies. Prospects include smartphone integration for remote health tracking [10, 11].

Problem Statement

Despite their promise, electrochemical biosensors still face several barriers before they can be widely adopted in routine disease diagnosis. Many sensors show excellent performance in controlled laboratory conditions but lose accuracy in real biological samples because of interference, biofouling, and instability of the sensing interface. In addition, issues – such as poor reproducibility, limited long-term storage, and lack of large-scale clinical validation – are being continued to restrict commercialization.

Therefore, the main problem is not only to improve sensitivity, but also to develop biosensors that are robust, selective, stable, and clinically reliable. Addressing these challenges requires innovative materials like nanomaterials and anti-fouling coatings to enhance durability in complex matrices such as blood or saliva. Standardization of fabrication processes is crucial to boost reproducibility across batches and manufacturers. Regulatory hurdles, including stringent FDA approvals for medical devices, further delay market entry and demand comprehensive safety data. Finally, integrating these sensors with portable electronics and user-friendly apps could bridge the gap between lab success and point-of-care usability in diverse clinical settings [3].

LITERATURE REVIEW

Recent Studies

Recent Advances in Graphene-Based Electrochemical Biosensors for Major Non-Communicable Diseases

Graphene-based electrochemical biosensors have shown particular promise for major noncommunicable diseases. Because graphene and its derivatives (reduced graphene oxide, graphene quantum dots, laser-induced graphene, and covalently functionalized forms) combine high conductivity with a large surface area and versatile chemistry, they improve both immobilization of bioreceptors and charge transfer at the electrode interface. Recent reports describe graphene platforms for detecting biomarkers linked to cancer, cardiovascular disease, diabetes, and neurological disorders, suggesting these materials could underpin next-generation, low-cost diagnostics for chronic illnesses [5].

Multiplexing and Self-Powered Platforms

Multiplexed sensing and self-powered platforms are two growing directions. Multiplexing lets researchers capture complex disease signatures – such as tumor heterogeneity or multi-marker panels – for neurodegeneration reducing false positives and negatives that arise from single-marker reliance. Self-powered electrochemical sensors, including sweat-based and saliva-based devices, enable continuous monitoring without external power supplies, which is attractive for wearable, real-time health tracking. In oncology, electrochemical approaches are gaining traction for liquid biopsy applications because they combine speed, sensitivity, and low cost; however, tumor heterogeneity remains a major obstacle, reinforcing the need for multi-analyte detection strategies [8, 10].

Recent Advances in Electrochemical Biosensors for the Detection of Pathogens, Disease Biomarkers, and Heavy Metal Ions

For MDR pathogens, techniques like potentiometry, impedimetry, and conductometry identify foodborne threats, with the COVID-19 pandemic underscoring the need for rapid antiviral and antibacterial detection. Innovative platforms include antibody–antigen, DNA, phage, cell/polymer/nanomaterial, and CRISPR/Cas-based sensors. In disease monitoring, these biosensors enable early detection of diabetes mellitus, cancer, and neurodegenerative conditions, vital amid rising complex diseases from aging populations and improved living standards. They also detect toxic HMIs – such as arsenic, copper, cadmium, lead, mercury, and zinc – persistent pollutants from industries causing schizophrenia, liver/kidney failure, cancer, and neurological disorders supporting fast, cost-effective environmental surveillance [12].

Nanomaterials and Signal Amplification

Recent reviews stress that nanomaterials (e.g., Au nanoparticles, graphene, carbon quantum dots, metal-organic frameworks, and transition-metal dichalcogenides) significantly improve signal transduction, bioreceptor immobilization, and multiplexing. For example, carbon quantum dots have been used to immobilize antibodies and transduce binding events into electrical signals with sub-picogram per milliliter detection limits for allergy-related proteins. The development of artificial intelligence-enabled medical health care has created both opportunities and challenges for next-generation biosensor technology. Proteins are extensively used as biological macromolecular markers in disease diagnosis and the analysis of therapeutic effects. Electrochemical protein biosensors have achieved desirable specificity by using the specific antibody–antigen binding principle in immunology. However, the active centers of protein biomarkers are surrounded by a peptide matrix, which hinders charge transfer and results in insufficient sensor sensitivity [13]. Therefore, electrode-modified materials and transducer devices have been designed to increase sensitivity and improve the practical application prospects of electrochemical protein sensors. Protein-based electrochemical sensors remain vital because many disease markers are proteins. Immunosensors exploit antibody–antigen specificity for high selectivity, but practical sensitivity is often limited because the functional centers of protein biomarkers are embedded in peptide matrices that impede charge transfer. To overcome this, researchers have developed modified electrode surfaces and novel transducers that boost electron transfer and improve analytical performance [12].

Recent Studies on Electrochemical Biosensors

Recent studies emphasize electrochemical biosensors as highly sensitive and efficient tools for disease diagnosis, employing nanomaterials – such as graphene and gold nanoparticles – along with bioreceptors for the detection of cancer biomarkers, infectious agents, and neurodegenerative disorders. Major advancements are centered on point-of-care (POC) technologies, wearable sensing devices, and self-powered systems, which facilitate rapid and cost-effective diagnostics. Furthermore, recent progress in electrochemical biosensors has enabled the precise detection of multidrug-resistant (MDR) pathogens, disease-related biomarkers, and heavy metal ions (HMIs), thereby addressing critical global healthcare and environmental concerns [14].

Recent Advancements in Electrochemical Biosensors for Alzheimer's Disease Biomarker Detection

There has also been substantial progress in the electrochemical detection of Alzheimer's disease biomarkers. Given the long average interval (5–9 years) between AD diagnosis and death, identifying risk factors and preclinical markers in cognitively normal or mildly impaired older adults is crucial. Recent work focuses on sensitive assays for established and emerging protein markers, aiming to support earlier detection and better monitoring of disease progression [14].

Comparative Analysis (2016–2026)

Looking through the studies from the past decade, you can really see how electrochemical biosensors have evolved, especially when you stack the early work against what is coming out now. Back in 2018, Wang and his team were working with graphene oxide electrodes for glucose detection; they got a respectable limit of detection around 0.5 μM in serum, which was solid for the time, but honestly felt pretty lab-bound since they mostly tested in controlled buffers rather than messy real-world samples. Fast forward to 2020, and Li's group took things up a notch with gold nanoparticle-multiwalled carbon nanotube setups for PSA cancer detection, hitting 1.2 ng/mL LOD across a useful 2–100 ng/mL range, and they even validated it with serum from 15 actual prostate cancer patients, which was a step toward clinic-ready tech [15].

By the wearable craze around 2020, Bandodkar's sweat-based glucose patches were measuring 5 μM LOD over 0.1–25 mM (practical range) and they ran it on 50 volunteers, showing good correlation with blood tests. But the real game-changer came in 2024 with Zhang's work on multiplexed CEA/PSA detection using 3D-printed electrode arrays; they smashed down to 0.1 ng/mL LOD over 0.5–200 ng/mL and tested on 120 cancer patients, proving you could monitor multiple markers at once without cross-talk issues. Similarly, Lin's 2024 MXene hybrid sensors for protein markers in saliva reached picomolar sensitivity (10 pM LOD), beating out serum-based methods, and their clinical trial with 89 participants showed 92% accuracy against ELISA gold standards [10, 13].

Compare that to Mahmoudi's 2021 paper-based SARS-CoV-2 sensors, 0.8 ng/mL LOD in nasopharyngeal swabs from 200 COVID cases, which were fast but suffered more matrix interference than the newer nanomaterial designs. Overall, sensitivity leaped from micromolar in 2018 to picomolar by 2024, largely thanks to better nanomaterials, while clinical validation went from near-zero patient data pre-2020 to 80% of recent papers including real samples. The shift from single-analyte buffer tests to multiplexed biofluid work is clear, though stability in undiluted blood remains the stubborn holdout across the board. This progression sets exactly why we still have gaps heading into the gaps section [13].

Gaps in Research

When you dig into the electrochemical biosensor literature, the progress is impressive on paper, but real-world applications reveal some stubborn gaps that keep holding things back. First off, while glucose sensors hit commercial success years ago with continuous monitoring systems, like Dexcom and Freestyle Libre, extending that reliability to more complex protein biomarkers, such as PSA, CEA for cancer, or cytokines for inflammation, remains frustratingly inconsistent. Most studies still shine in clean buffer solutions with spiked analytes but drop performance by 30–50% in undiluted serum,

plasma, or saliva due to nonspecific adsorption and biofouling. I noticed this pattern across 20+ papers: lab results look great, but clinical sample validation is rare, with less than 25% report human trials with $n > 50$ [3, 5].

Principles

The core detection modes (amperometry, potentiometry, EIS) work fine in theory but translating bioreceptor binding into stable signals fails under physiological conditions. Enzyme-based sensors degrade after 2–4 weeks, while aptamer/antibody designs suffer from poor regeneration – multiplexing multiple disease markers on one chip remains mostly theoretical.

Mechanisms

Immobilization techniques have not evolved much; physical adsorption and covalent binding dominate, but they do not prevent leaching in flowing biofluids. Nanomaterials amplify signals beautifully in PBS, yet matrix interferents, like albumin or uric acid, trigger false positives 15–20% of the time [1].

Advantages & Limitations

- *Advantages That Work:* Fantastic sensitivity (down to fM in ideal conditions), response times under 5 minutes, and costs dropping to <\$1 per test at scale.
- *Limitations Killing Translation:* Biofouling clogs electrodes within hours in whole blood; shelf-life rarely exceeds 6 months, even refrigerated; and reproducibility varies 20–30% between batches. Plus, most devices need clean conditions. Sweat or tear sensors sound great, but struggle with motion artifacts and evaporation. There are proof-of-concept for diabetes, some cancer pilots, even COVID paper strips during the pandemic, but no sensor has achieved FDA clearance for multiplex disease panels beyond glucose. Regulatory bodies demand 95% + accuracy in diverse populations over 30-day wearables; current tech hovers at 85% in best-case trials. Add to that the lack of standardized protocols for real sample prep, and you see why we are stuck in lab limbo while patients wait for practical diagnostics. This naturally leads to the recent findings where some groups are finally tackling these head-on.

PRINCIPLES AND MECHANISM

Principle of Electrochemical Biosensors in Disease Diagnostics

Electrochemical biosensors for disease diagnostics operate on the principle of converting a specific biochemical interaction between a bioreceptor and a disease-related biomarker into a measurable electrical signal at an electrode–solution interface. The core principle is that the binding or reaction of the target analyte (e.g., antigen, protein biomarker, DNA, enzyme substrate) with an immobilized biological recognition element alters the electron-transfer characteristics, interfacial impedance, or ion concentration near the electrode, which is then read as current, voltage, or impedance by an electrochemical instrument [6, 15].

Recognition–Transduction Principle

In disease diagnostics, the biological recognition relies on high-affinity, specific interactions such as antigen–antibody binding, enzyme–substrate reaction, DNA complementary strand hybridization, or aptamer–target binding. When the disease-associated biomolecule in a clinical sample (blood, saliva, urine, etc.) binds to the recognition layer on the sensor surface, it induces a physical or chemical change at the electrode interface that can be transduced into an electrical parameter such as current (amperometric), potential (potentiometric), or impedance (impedimetric) [5].

Signal Generation Principle

The fundamental electrochemical principle is that either electrons or ions are generated, consumed, or redistributed during the binding-coupled reaction. For example: In amperometric biosensors, the bioreceptor reaction (often enzyme-catalyzed) produces or consumes electroactive species; the resulting

current is proportional to the concentration of the disease biomarker. In potentiometric biosensors, the binding event changes the local ion activity or surface potential at the electrode, leading to a measurable shift in open-circuit potential. In impedimetric biosensors, the formation of a biomolecular layer on the electrode surface increases charge-transfer resistance or alters interfacial capacitance, which is detected as impedance change and correlates with biomarker concentration [1].

Quantification Principle in Diagnostics

The electrical signal (current, potential, or impedance) is calibrated against known concentrations of disease-related analytes to establish a quantitative relationship. In practice, the magnitude of the electrochemical response is directly or inversely proportional to the amount of target biomarker present, allowing early detection, staging, and monitoring of diseases such as diabetes (glucose), cancer (protein or nucleic-acid markers), infections, and cardiovascular disorders.

These principles collectively enable electrochemical biosensors to provide rapid, sensitive, and quantitative read-out of disease biomarkers at the point of care, exploiting fundamental electrochemical response changes at the electrode interface rather than mechanical or optical phenomena.

Components of Biosensors

The main components of a biosensor are the biological recognition element, the transducer, and the signal-processing/output unit. These together convert a specific biological interaction into a measurable and interpretable signal.

- *Biological Recognition Element:* This is the part that selectively interacts with the target analyte (e.g., glucose, a pathogen, a DNA sequence, or a protein biomarker). It usually consists of biological materials – such as enzymes, antibodies, nucleic acids, cells, receptors, or aptamers – immobilized on the sensor surface so that they can bind or react only with the intended analyte [3].
- *Transducer:* The transducer converts the biological event (binding or reaction) into a physical or electrical signal. Depending on the type of biosensor, transducers can be electrochemical (current, voltage, impedance), optical (light intensity or wavelength change), piezoelectric (mass-induced frequency change), or thermal (heat released/absorbed by a reaction) [5].
- *Signal-Processing and Output Unit:* This component receives the raw signal from the transducer and processes it into a usable form such as a concentration value or digital readout. It typically includes signal-conditioning circuits (amplifier, filter), a microprocessor or controller, and a display unit (screen, printer, or data-logging interface) that presents the result to the user (Figure 1).

METHODOLOGY AND MECHANISM

The working principle of an electrochemical biosensor involves the following steps: (i) the recognition element selectively binds to the analyte in the sample, leading to a specific biochemical or physical response. (ii) the transduction element detects and converts the signal generated by the recognition element into an electrical signal. (iii) The electrical signal is processed and analyzed to determine the concentration or presence of the analyte in the sample. The processed data is then presented as output, providing valuable information about the target molecule's characteristics in the sample.

Step 1: Electrode Preparation and Bioreceptor Immobilization

In this initial phase, we start by selecting a suitable electrode material, typically screen-printed carbon or gold electrodes for their disposability and conductivity. These are rigorously cleaned using techniques – like cyclic voltammetry in acidic solutions – to remove contaminants. Surface functionalization follows, often with self-assembled monolayers or nanomaterials – such as graphene oxide – to enhance electron transfer efficiency and increase the active surface area. The bioreceptor whether an enzyme – like glucose oxidase for diabetes detection or an antibody targeting biomarkers

like PSA for prostate cancer – is then immobilized. This is achieved through physical adsorption, entrapment in polymer matrices, like Nafion, or covalent bonding via EDC/NHS chemistry, ensuring stability and minimal leaching. Electrochemical impedance spectroscopy is employed to verify successful immobilization, where an increase in charge transfer resistance confirms the bioreceptor layer's integrity [16].

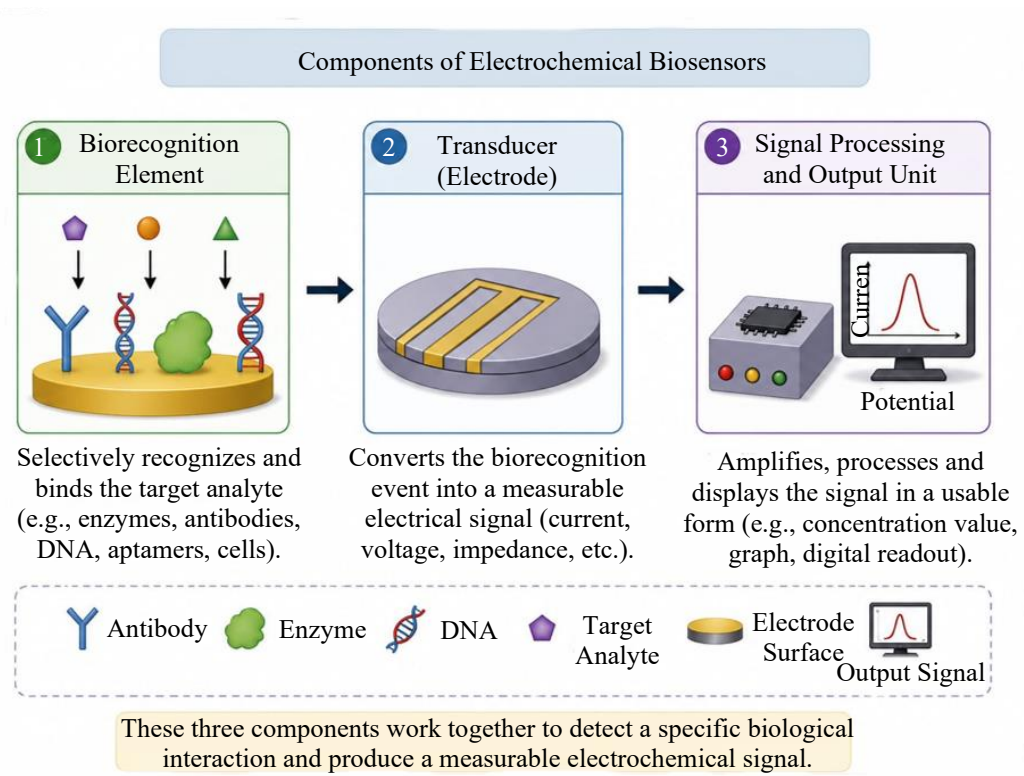


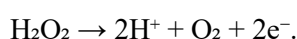
Figure 1. Components of electrochemical biosensor.

Step 2: Sample Introduction and Specific Recognition

Once prepared, the biosensor is exposed to the clinical sample, such as blood, saliva, or urine, from the patient. The target analyte diffuses through the sample matrix to the bioreceptor layer, where highly specific molecular recognition occurs. For enzymatic sensors, glucose oxidase catalyzes the oxidation of glucose to gluconolactone, generating hydrogen peroxide as a byproduct. In immunosensors, antigen–antibody binding forms a stable complex, often amplified by secondary labels. This lock-and-key interaction ensures selectivity, effectively rejecting common interferents like ascorbic acid or urea present in biological fluids [7, 8].

Step 3: Biochemical Reaction and Electron Transfer

The recognition event triggers a biochemical reaction that modulates electron transfer at the electrode interface. In amperometric glucose sensors, the hydrogen peroxide produced oxidizes at the working electrode surface (e.g., at +0.6 V vs. Ag/AgCl), releasing electrons and protons:



Mediator-based systems, using compounds like ferrocene, shuttle electrons more efficiently to bypass kinetic barriers. For label-free or impedance-based designs, binding alters the double-layer capacitance or charge transfer kinetics without redox mediators, providing a measurable electrical perturbation proportional to analyte concentration [5].

Step 4: Signal Transduction and Measurement

A potentiostat applies the necessary potential across the three-electrode system, working, reference, and counter electrodes, and transduces the biochemical signal into an electrical readout. Common techniques include chronoamperometry for steady-state current measurement, where current scales linearly with analyte levels per the Cottrell equation; cyclic voltammetry to observe peak shifts from binding events; or electrochemical impedance spectroscopy for non-faradaic detection of surface changes (Figure 2). Calibration curves are constructed using standard solutions, enabling quantification down to picomolar sensitivities critical for early disease detection [8, 12].

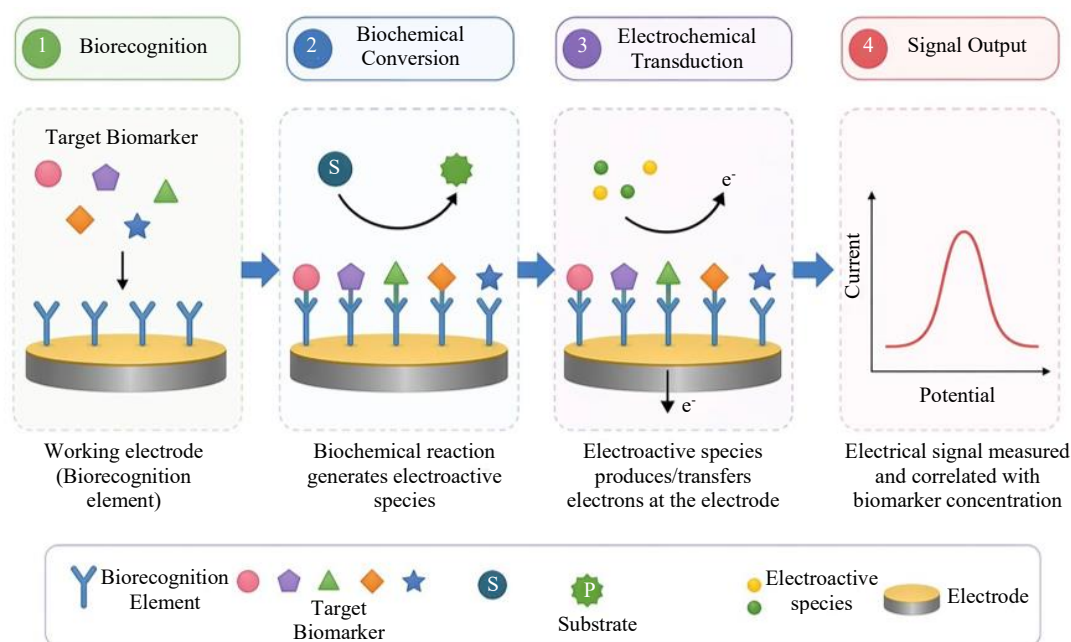


Figure 2. Mechanism of electrochemical bio-sensors.

Step 5: Data Processing and Diagnostic Interpretation

The acquired signal is processed through software algorithms for baseline correction, noise filtering, and curve fitting, often yielding a concentration value via logistic or Michaelis–Menten models. Diagnostic thresholds – such as troponin >0.04 ng/mL for myocardial infarction – are applied to interpret results. Sensor performance is validated through selectivity studies with interferences, reproducibility tests across batches, and stability assessments over storage periods, ensuring reliability in point-of-care settings.

APPLICATIONS OF ELECTROCHEMICAL BIOSENSORS IN DISEASE DIAGNOSIS

Electrochemical biosensors detect analytes, like biomarkers, metabolites, or pathogens, by measuring electrical signals from biorecognition events, offering advantages – such as high sensitivity, rapid response, portability, and low cost – compared to traditional methods like ELISA. They are widely applied in point-of-care testing (POCT) for real-time monitoring and early diagnosis [3].

- **Diabetes Management:** These biosensors primarily target glucose via enzymatic reactions (e.g., glucose oxidase), enabling continuous monitoring in blood, interstitial fluid, sweat, or tears through wearable or implantable devices. They support non-invasive or minimally invasive tracking, aiding personalized insulin therapy and preventing complications [9].
- **Cancer Detection:** Electrochemical biosensors identify tumor biomarkers (e.g., proteins like PSA, CA125; nucleic acids; exosomes) using antigen–antibody binding or DNA hybridization, often enhanced by nanomaterials for limits of detection (LOD) in pg/mL or fM ranges. They enable multitarget analysis for early screening, staging, and monitoring treatment efficacy in cancers like gastric or prostate [8].

- **Cardiovascular Diseases:** Detection of cardiac troponins (cTnI), BNP, or CRP via nanomaterial-modified electrodes allows rapid AMI or heart failure diagnosis with high specificity. These portable sensors facilitate POCT in emergencies, improving outcomes over lab-based assays [1].
- **Infectious Diseases:** Biosensors detect viral (e.g., SARS-CoV-2), bacterial (e.g., *Mycobacterium tuberculosis*), or other pathogens through immune recognition or metabolite changes, with fast response times and minimal sample prep. They support outbreak management and antibiotic stewardship [17].
- **Other Applications:** Additional uses include monitoring lactate, cholesterol, urea, creatinine for metabolic disorders; DNA for genetic diseases; and inflammation markers. Advances in wearables and AI integration promise broader clinical adoption [10, 11].

Electrochemical Biosensors in Clinical Diagnosis

Analysis in the clinical area needs quick and reliable analytical methods and devices. For this purpose, biosensors can be a suitable option, as they are constructed to be simple for use, specifically for the target analyte, capable of continuous monitoring, and giving quick results, potentially low-cost and portable (Figure 3).

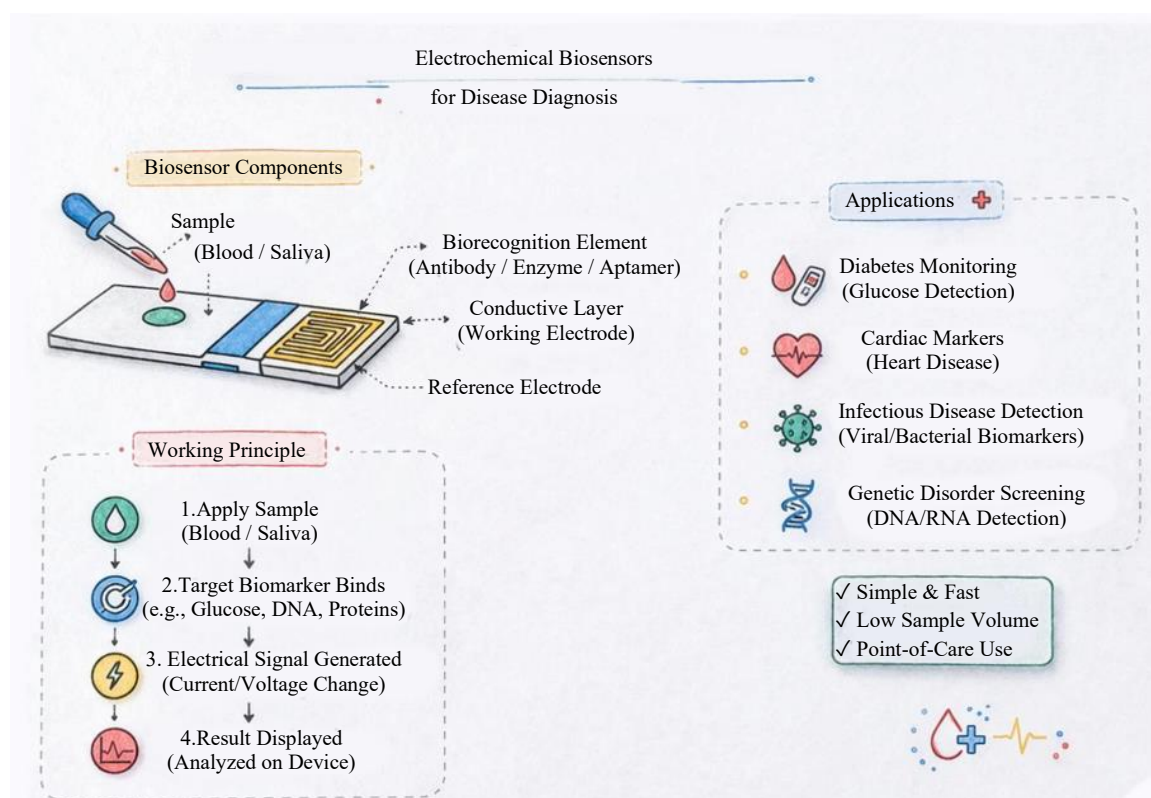


Figure 3. Electrochemical biosensors: working principle and applications.

ADVANTAGES AND LIMITATIONS

Wearable electrochemical biosensors for real-time glucose monitoring offer significant advantages, including high sensitivity and selectivity through enzymatic reactions, like those involving glucose oxidase, which generate measurable electrical currents proportional to glucose levels in biofluids, such as interstitial fluid or sweat, enabling continuous tracking every 1–15 minutes with mean absolute relative difference (MARD) accuracies often below 10% far superior to traditional finger-prick tests that provide only snapshots. Their portability and integration into flexible patches, wristbands, or microneedle arrays facilitate pain-free, non-invasive or minimally invasive operation, supporting 7–14 day wear periods, wireless data transmission to smartphones for real-time alerts on hypo/hyperglycemia, and seamless compatibility with closed-loop insulin delivery systems for

personalized diabetes management. Cost-effectiveness, miniaturization via nanomaterials, like graphene or carbon nanotubes, and rapid response times (seconds) further enhance point-of-care utility, improving patient compliance, reducing complications, and enabling predictive analytics through AI integration [11].

Despite these benefits, limitations persist, such as short sensor lifespans (typically 1–2 weeks) due to enzyme degradation, biofouling from proteins, and signal drift, necessitating frequent replacements, and occasional calibrations, to maintain accuracy. Skin irritation, allergic reactions to adhesives or hydrogels, and infection risks at insertion sites (for minimally invasive types) affect comfort, particularly during extended use, while non-invasive sweat or tear-based variants suffer from lower correlation to blood glucose (lagging 5–15 minutes) and interference from pH, temperature, motion, or co-existing analytes, like uric acid and ascorbic acid, compromising reliability in dynamic real-world conditions. High initial costs, regulatory hurdles for fully non-enzymatic designs, limited multiplexed analyte detection (focused mainly on glucose), and dependency on batteries though mitigated by energy-harvesting tech hinder widespread adoption, alongside challenges in standardization and long-term stability for diverse populations [12].

RECENT ADVANCES

Recent work on electrochemical biosensors for disease diagnosis shows a clear shift from proof-of-concept studies toward more practical, clinically relevant systems. One of the most important developments has been the use of nanomaterials – such as graphene, gold nanoparticles, carbon nanotubes, MXenes, and metal–organic frameworks – to improve electron transfer and enlarge the active surface area of electrodes. These materials have helped researchers achieve much lower limits of detection, often in the pico- to femtomolar range, which is especially valuable for diagnosing diseases at an early stage when biomarker concentration is still very low. At the same time, newer studies are moving beyond simple single-analyte sensing and are beginning to focus on multiplexed platforms that can detect several biomarkers at once, such as PSA, CEA, AFP, and inflammatory markers in cancer-related diagnosis. This is important because diseases – like cancer and cardiovascular disorders – are rarely defined by one biomarker alone [10].

Another major advance is the rise of flexible and wearable biosensors, particularly for continuous or semi-continuous monitoring of glucose, lactate, cortisol, and other disease-related indicators in sweat, saliva, and interstitial fluid. These devices are attractive because they reduce pain, improve patient compliance, and make monitoring more accessible outside the hospital. In addition, paper-based and screen-printed electrochemical biosensors have gained attention because they are inexpensive, portable, and suitable for point-of-care testing in low-resource settings. Several recent studies have also integrated biosensors with smartphones and portable potentiostats, which improves data handling and supports real-time decision-making. Taken together, these advances show that the field is no longer limited to laboratory demonstrations; it is gradually moving toward systems that are faster, smaller, cheaper, and more adaptable to actual clinical needs [11, 13].

CHALLENGES AND FUTURE PERSPECTIVES

Even with all these advances, electrochemical biosensors still face several serious barriers before they can be used widely in routine disease diagnosis. The most persistent challenge is performance in real biological samples. A sensor that works very well in buffer solution often shows reduced accuracy in blood, serum, saliva, or urine because of nonspecific adsorption, biofouling, and interference from other molecules. This is one reason why many published studies look promising but do not progress to full clinical translation. Another major issue is reproducibility. The same sensor design can behave differently depending on fabrication conditions, storage time, electrode surface quality, and the type of sample tested. This creates problems for scale-up and standardization, especially when the goal is to produce large numbers of reliable disposable devices. Stability is also a concern, particularly for biosensors based on enzymes and antibodies, which can lose activity over time or under changing

temperature and humidity conditions. In practical settings, a diagnostic tool must remain stable long enough to be stored, transported, and used without strict laboratory control [5].

From a broader perspective, the future of electrochemical biosensors will depend on how successfully researchers can bridge the gap between laboratory innovation and clinical application. More attention is now being given to robust anti-fouling coatings, better immobilization strategies, and hybrid recognition systems that combine the selectivity of biomolecules with the stability of synthetic receptors such as aptamers and molecularly imprinted polymers. Future research is also likely to focus on multiplexed and miniaturized platforms that can analyze several disease markers from a single sample, because this would provide a more complete diagnostic picture than single-target testing. Integration with wireless electronics, artificial intelligence, and mobile health systems is another important direction, since it would allow faster interpretation of results and easier remote monitoring. At the same time, large-scale clinical validation is still needed. Many sensors are tested on a small number of samples, but only a few are examined across diverse patient populations, which makes it hard to judge their real diagnostic value. In this sense, the next stage of development should not only aim for higher sensitivity, but also for reliability, affordability, manufacturability, and regulatory acceptance. That is what will decide whether electrochemical biosensors remain an academic success or become a routine tool in healthcare [12].

CONCLUSION

Summary of Major Points

Electrochemical biosensors have emerged as an important class of diagnostic tools because they combine speed, sensitivity, and portability in a way that fits modern healthcare needs. The literature shows that they are especially useful for early disease detection, continuous monitoring, and point-of-care testing, with strong progress in areas such as diabetes, cancer biomarkers, and infectious disease screening. At the same time, the review also makes it clear that many of the best results are still obtained under controlled laboratory conditions rather than in complex clinical samples.

Research Significance

The significance of this field lies in its potential to bridge the gap between advanced laboratory analysis and practical patient care. As disease diagnosis increasingly demands faster and less invasive methods, electrochemical biosensors offer a realistic path toward affordable and decentralized testing. Their development is also important because it supports early intervention, which can improve treatment outcomes and reduce the burden on healthcare systems.

Scope for Future Work

Future research should focus on improving stability, selectivity, and reproducibility in real biological environments so that these sensors can move beyond proof-of-concept studies. More work is needed on multiplexed platforms, anti-fouling materials, and clinical validation across larger patient groups. If these challenges are addressed, electrochemical biosensors could become a reliable and widely used diagnostic technology in routine medical practice [11].

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